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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,679	03/11/2005	Thomas Felzmann	4518-0101PUS1	7223
2292 7590 01/12/2007 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			EXAMINER XIE, XIAOZHEN	
			ART UNIT	PAPER NUMBER
			1646	
SHORTENED STATUTORY PERIOD OF RESPONSE		NOTIFICATION DATE	DELIVERY MODE	
3 MONTHS		01/12/2007	ELECTRONIC	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/12/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

# Office Action Summary

Application No.

10/527,679

Applicant(s)

FELZMANN, THOMAS

Examiner

Xiaozhen Xie

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 10-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 20050311.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Status of Application, Amendments, And/Or Claims*

The Information Disclosure Statement (IDS) filed 11 March 2005 has been entered in full. Applicant's amendment of the claims received on 29 September 2006 is acknowledged.

### *Election/Restrictions*

Applicant's election with traverse of Group I, claims 1-9, in the reply filed on 29 September 2006 is acknowledged. The restriction election was further confirmed in a telephonic interview with Leonard Svensson on 20 November 2006 because the 29 September 2006 response appears to have a typo error indicating "Group II, claims 1-9". The traversal is on the ground that the Ebner et al. reference does not teach "loading DCs with an antigen against a specific tumor", nor teaches "IL-12 release by the combined stimulation of tumor antigen loaded DCs with LPS and IFN- $\gamma$ ". Applicant's argument has been fully considered but has not been found to be persuasive. As set forth in the previous office action, Ebner et al. teach preloading tumor or non-tumor bearing mice with tumor antigen, i.e., by immunization with tumor antigen or super-antigen (column 25, lines 22-62). The tumor antigen administered into the mice will be exposed and loaded into DCs. Further, Ebner et al. teach dendritic cells release IL-12 when stimulated with LPS (column 57, lines 56-67). Even though Ebner et al. do not express co-stimulation with LPS and IFN- $\gamma$ , IFN- $\gamma$  is present in the circulation system since PBLs (both resting and active) secrete IFN- $\gamma$  (see Fig. 9). Since the claim does not

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require DCs to be loaded and treated *in vitro*, i.e., in isolated and cultured cells, Ebner et al. teach the limitations of claim 1. Thus the technical feature of Group I lacks novelty or inventive step and does not make a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-16 are pending. Claims 10-16 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-9 are under examination.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Felzmann et al. (Cancer Letters, 2001, July 26, Vol. 168:145-154) ("Felzmann (2001)").

The instant claims are directed to a method for the treatment of a tumor, which comprises administering to a patient active dendritic cells (DCs) releasing IL-12 which are loaded with an antigen against a specific tumor, and upon treatment with LPS and IFN- $\gamma$ , release IL-12 (claim 1), wherein the tumor is an advanced malignancy (claim 3), DCs are taken from the patient having the tumor or from a bone marrow donor (claim 4), the tumor antigen is from a tumor cell of the patient (claim 5), and DCs are generated *in vitro* from PBMCs (claim 9).

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Felzmann (2001) teaches that tumor antigen pulsed DCs can induce anti-tumor immunity and they have been used in tumor vaccination clinical trials (pp. 145, Abstract and Introduction 2<sup>nd</sup> paragraph) (claim 1). Felzmann (2001) teaches that release of IL-12 is an important mediator of anti-tumor immunity (pp. 145, Abstract), and that DCs matured by stimulation with CD40L or LPS in conjunction with IFN- $\gamma$  release IL-12 (pp. 147, Materials and Methods, section 2.3. and pp. 151, Figure 4) (claim 1). Felzmann (2001) teaches advanced tumors such as human neuroblastoma (pp. 147, Materials and Methods, section 2.1.) (claim 3), and DCs were prepared in vitro from peripheral blood mononuclear cells (pp. 147, Materials and Methods, section 2.3.) (claim 9). Felzmann (2001) teaches that it might be feasible to use matured DCs for the in vitro expansion of antigen-specific T lymphocytes using soluble target cell lysates, which can be prepared from any type of tumor, and such DCs could be applied directly as a tumor vaccine (pp. 153, let column, last paragraph in Discussion) (claims 4 and 5). Therefore, Felzmann (2001) anticipates the claimed invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Felzmann (2001), in view of Asavaroengchai et al. (PNAS, 2002, Jan. 22, Vol. 99:931-936).

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Felzmann (2001) teaches as set forth above. Felzmann (2001), however, does not teach that the treatment is performed after bone marrow transplantation (claim 2).

Asavaroengchai teaches that bone marrow transplants (BMT) or peripheral stem cell transplants are currently being used for the treatment of hematopoietic and solid tumors, and combining suitable immunization approaches with BMT can overcome tumor induced defects in the host anti-tumor immune response. Asavaroengchai teaches that in a therapeutic setting tumor antigen-pulsed DCs can have an impact on residual tumor that remains following BMT (pp. 931, see Abstract and Introduction).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Felzmann (2001), with those of Asavaroengchai to perform the treatment after bone marrow transplantation. One of ordinary skill in the art would have been motivated to combine the teachings, because Felzmann (2001) teaches a method of immune therapy using tumor antigen pulsed dendritic cells (DCs) that release IL-12 upon maturation with LPS and IFN- $\gamma$ , Asavaroengchai teaches that tumor-pulsed DCs can have impact on residual tumor that remains following BMT. Therefore, the teachings provide a reasonable expectation of successfully treating a tumor in a patient.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felzmann (2001), in view of Rieser (Urol. Int., 1999, Vol. 63(3):151-159), and further in view of Felzmann et al. (Cancer Letters, 2000, Vol. 161:241-250) ("Felzmann (2000)").

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Felzmann (2001) teaches as set forth above, a method for the treatment of a tumor, comprising administering to a patient active DCs, which are loaded with an antigen against a specific tumor, and upon stimulating with LPS and IFN- $\gamma$ , release IL-12.

Felzmann (2001), however, does not teach that the DCs are additionally charged with a tracer antigen (claim 6) that is keyhole limpet hemocyanine (KLH) (claim 7), or additionally charged with an adjuvant tetanus toxoid (claim 8).

Rieser teaches using KLH as a tracer molecule for the determination of the magnitude, kinetics, and T-helper type-1 bias of the cellular and humoral immune response induced by DCs-based immunization (pp. 151, see Abstract).

Felzmann (2000) teaches Xenogenization by tetanus toxoid (TT) loading into human tumor cells for anti-tumor immune therapy (pp. 241, Abstract). Felzmann (2000) teaches that unresponsiveness to tumor associated antigens (TAAs) could be overcome when a mixture of TAAs was used together with class II restricted peptides from TT for cell pulsing in vitro (pp. 241, Introduction, 1<sup>st</sup> paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Felzmann (2001), with those of Rieser and Felzmann (2000) to additionally load DCs with a tracer antigen KLH and an adjuvant tetanus toxoid. One of ordinary skill in the art would have been motivated to combine the teachings, because Felzmann (2001) teaches a method of immune therapy using tumor antigen pulsed dendritic cells (DCs) that release IL-12 upon maturation with LPS and IFN- $\gamma$ , Rieser teaches using KLH as a tracer molecule for determination of the

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kinetics of the immune therapy, and Felzmann (2000) teaches tetanus toxoid (TT) loading into human tumor cells enhances responsiveness to tumor associated antigens. Therefore, the teachings provide a reasonable expectation of successfully treating a tumor in a patient.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for the recitation "due to treatment with lipopolysaccharide (LPS) and interferon-gamma (IFN- $\gamma$ ), release IL-12". There is no technical characterization, e.g., time frame, for the treatment, nor amount of IL-12 release is defined.

Claim 4 recites "the bone marrow donor" according to claim 1. There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Objections***

Claim 1 is objected to because of the following informalities:

Claim 1 has a grammar error for reciting "administering to a patient in need of such treatment and effective amount of". It should be "administering to a patient in need of such treatment an effective amount of".

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Appropriate correction is required.

**Conclusion**

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph. D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph. D.  
December 19, 2006



EILEEN B. O'HARA  
PRIMARY EXAMINER